Case Report

Underuse of Thrombolytic Therapy in Acute Myocardial Infarction and Left Bundle Branch Block

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ABSTRACT

Thrombolytic therapy reduces mortality in patients with acute myocardial infarction (AMI) and left bundle branch block (LBBB). The difficulty in accurately diagnosing AMI in patients with LBBB, however, might result in their undertreatment. Among 3,890 patients hospitalized with chest pain, 241 (6.2%) had LBBB at presentation. The only variable independently associated with AMI among patients with LBBB was in-hospital left ventricular failure (odds ratio [OR]: 4.32, 95% confidence interval [CI]: 1.95–9.57, $p<0.0005$). Only 16 (29%) of the LBBB patients with AMI received thrombolytic therapy compared with 583 (78%) of the 747 patients with ST-elevation AMI ($p<0.0005$). A further 19 (10%) LBBB patients without AMI also received thrombolysis. Difficulty in making an accurate early diagnosis in patients with LBBB ensures that the majority of those with AMI fail to receive thrombolytic therapy while others without AMI are treated inappropriately. Improved diagnostic and therapeutic strategies are needed for patients with acute coronary syndromes and LBBB.

Key words: thrombolytic therapy, acute myocardial infarction, left bundle branch block

Introduction

Left bundle branch block (LBBB) confers an adverse prognosis in patients with acute myocardial infarction (AMI).[1,2] Randomized trials have shown that this high risk subgroup derives particular prognostic benefit from thrombolytic therapy.[3] Electrocardiographic criteria for the diagnosis of AMI in the presence of LBBB, however, have low sensitivity,[4–6] and cardiac biomarker concentrations are rarely available when treatment decisions are made. Patients with chest pain and LBBB, therefore, pose a diagnostic and therapeutic dilemma to which the decision of whether or not to administer thrombolysis is central. The aims of this study were a) to measure rates of enzymatically-defined AMI in patients presenting with LBBB, b) to measure rates of thrombolytic therapy administration in patients with LBBB and AMI, and c) to identify clinical characteristics associated with AMI in patients with LBBB.

Methods

Patient Population

Clinical characteristics were recorded prospectively in 4,284 consecutive patients with chest pain admitted to 3 East London coronary care units from January 2000 to November 2002. Readmissions during the study period were excluded. Data included demographics, cardiac history, risk factors, cardiac biomarker concentrations, details of treatment, diagnosis, and major in-hospital complications. The presenting electrocardiogram (ECG) findings were available for 3,890 (91%) patients. LBBB was diagnosed in the presence of sinus or supraventricular rhythm if the QRS duration was ≥120 ms with a QS or rS complex in lead V_1, and an R-wave peak time of ≥60 ms in lead I, V_5 or V_6 associated with the absence of a Q-wave in the same lead. AMI was defined by the World Health Organization (WHO) criteria (a rise in serum creatinine kinase concentration [CK] to ≥400 IU/l, upper limit of reference range: 200 IU/l) to conform with the evidence base for thrombolytic therapy in LBBB. In the presence of LBBB, the administration of thrombolysis was recommended when the conduction disorder was new, or when AMI was suspected on clinical grounds. There was no primary percutaneous coronary intervention (PCI) service during the study period. Left ventricular failure (LVF) was diagnosed in the presence of crepitations at the lung bases together with radiological evidence of interstitial or alveolar edema requiring diuretic therapy.

Statistical Analysis

Clinical characteristics were analyzed in relation to the presence or absence of LBBB at presentation. Thrombolysis administration and clinical characteristics within the subgroup of patients with LBBB were analyzed in relation to enzymatically-defined AMI. Continuous data were

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Table 1. Baseline characteristics of patients with and without left bundle branch block

Variable	Study cohort n = 3,890	LBBB n = 241	Non-LBBB n = 3,649	p*
Age (years)	62.0±13.7	69.1±10.9	61.5±13.7	<0.0005
Males	2,646 (68.0%)	155 (64.3%)	2,491 (68.3%)	0.203
Caucasian	2,333 (61.9%)	158 (67.5%)	2,175 (61.5%)	0.065
Diabetes mellitus	1,018 (26.2%)	80 (33.2%)	938 (25.7%)	0.01
Hypertension	1,850 (47.6%)	132 (54.8%)	1,718 (47.1%)	0.021
Current smoker	1,263 (32.8%)	45 (18.8%)	1,218 (33.7%)	<0.0005
Preceding angina	1,197 (30.8%)	95 (39.4%)	1,102 (30.2%)	0.003
Previous myocardial infarction	964 (24.9%)	99 (41.1%)	865 (23.8%)	<0.0005
Previous unstable angina	1,133 (29.3%)	88 (36.5%)	1,045 (28.8%)	0.011
Previous acute coronary syndrome	1,657 (42.8%)	154 (63.9%)	1,503 (41.4%)	<0.0005
Previous angioplasty	489 (12.6%)	34 (14.1%)	455 (12.5%)	0.458
Previous CABG	314 (8.1%)	42 (17.4%)	272 (7.5%)	<0.0005
Previous revascularization	689 (17.7%)	60 (24.9%)	629 (17.2%)	0.003
Aspirin	1,847 (47.9%)	153 (64.3%)	1,694 (46.8%)	<0.0005
Beta-blocker	922 (23.9%)	49 (20.5%)	873 (24.1%)	0.203
ACE inhibitor	858 (22.2%)	107 (44.8%)	751 (20.8%)	<0.0005
Statin	962 (25.0%)	66 (27.7%)	896 (24.8%)	0.564
Diuretic	805 (20.9%)	123 (51.7%)	682 (18.9%)	<0.0005

Data are presented as mean±standard deviation (continuous variables) or frequency (categorical variables). *LBBB versus non-LBBB *Abbreviations:* ACE = angiotensin converting enzyme CABG = coronary artery bypass graft surgery LBBB = left bundle branch block.

compared by the Mann-Whitney U test and categorical data by the chi-square test. Logistic regression analyses incorporating variables with univariate significance <0.1 were performed to account for possible confounding factors with LBBB and with AMI. All statistical analyses were performed using SPSS 11.5 for Windows (SPSS Inc., Chicago, Illinois, USA).

Results

Baseline characteristics of the study cohort are shown in Table 1. Of the 3,890 patients, 241 (6.2%) had LBBB at presentation. These patients were older, more frequently had a history of diabetes, hypertension, and coronary revascularization, and took more cardioactive drugs than patients without LBBB. Factors independently associated with LBBB in logistic regression analysis were age ≥60 years (OR: 1.66, 95% CI: 1.16–2.38), previous coronary artery bypass surgery (OR: 2.02, 95% CI; 1.11–3.70), background angiotensin converting enzyme inhibitor therapy (OR: 1.80, 95% CI: 1.32–2.47), diuretic therapy (OR: 2.31, 95% CI: 1.69–3.16), admission heart rate>100/min (OR: 1.73, 95% CI: 1.22–2.45), serum creatinine concentration>120 μmol/L (OR: 1.55, 95% CI: 1.13–2.12), and in-hospital LVF (OR: 2.09, 95% CI: 1.48–2.97).

A total of 55 (23%) patients with LBBB had AMI confirmed by CK ≥400 IU/l. In this group, rates of LVF (62% versus 24%, p<0.0005) and hospital death (13% versus 1%, p<0.0005) were substantially higher than in patients without AMI. A number of variables showed univariate association with AMI (Table 2) but only the development of in-hospital LVF was independently associated with AMI among patients with LBBB, with an odds ratio for AMI of 4.32 (95% CI: 1.95–9.57, p<0.0005) compared with patients without LVF.

Only 16 (29%) of 55 LBBB patients with confirmed AMI received thrombolytic therapy compared with 583 (78%) of the 747 patients with ST-elevation AMI (p<0.0005). A further 19 (10%) patients with LBBB but without AMI also received thrombolysis. Rates of thrombolytic therapy in troponin +ve

Table 2. Characteristics of left bundle branch block patients with and without acute myocardial infarction

Variable	AMI n = 55*	Non-AMI n = 184*	p
Age (years)	69.3±10.5	68.8±10.9	0.847
Males	41 (74.5%)	114 (62.0%)	0.086
Caucasian	40 (74.1%)	117 (65.7%)	0.251
Diabetes mellitus	19 (34.5%)	60 (32.6%)	0.789
Hypertension	22 (40.0%)	109 (59.2%)	0.012
Current smoker	14 (25.9%)	31 (16.9%)	0.139
Preceding angina	12 (21.8%)	82 (44.6%)	0.002
Previous myocardial infarction	22 (40.0%)	75 (40.8%)	0.920
Previous unstable angina	12 (21.8%)	75 (40.8%)	0.010
Previous acute coronary syndrome	29 (52.7%)	123 (66.8%)	0.056
Previous angioplasty	4 (7.3%)	30 (16.3%)	0.092
Previous CABG	8 (14.5%)	34 (18.5%)	0.501
Previous revascularization	10 (18.2%)	50 (27.2%)	0.177
Aspirin	32 (58.2%)	120 (66.3%)	0.271
Beta-blocker	5 (9.1%)	44 (24.2%)	0.015
ACE inhibitor	22 (40.0%)	84 (46.2%)	0.421
Statin	17 (30.9%)	49 (27.1%)	0.579
Diuretic	27 (49.1%)	94 (51.9%)	0.712
Atrial fibrillation or flutter	7 (12.7%)	24 (13.1%)	0.940
Heart rate	93±24	87±27	0.028
Systolic BP (mm Hg)	135±32	146±29	0.007
Diastolic BP (mm Hg)	81±19	82±18	0.551
Serum [creatinine] (μmol/l)	153±110	119±61	0.001
Serum [glucose] (mmol/l)	11.3±6.7	9.4±5.5	0.019
Peak [creatinine kinase] (IU/l)	1428±2375	128±83	<0.0005
Thrombolysis administered	16 (29.1%)	19 (10.3%)	0.001
Left ventricular failure	34 (61.8%)	44 (24.2%)	<0.0005
Ventricular fibrillation	8 (14.5%)	0 (0%)	<0.0005
Death	7 (12.7%)	2 (1.1%)	<0.0005

Data are presented as mean±standard deviation (continuous variables) or frequency (categorical variables). *Two (0.8%) of 241 patients had no serial (creatinine kinase) measurements available. *Abbreviations:* ACE = angiotensin converting enzyme; AMI = acute myocardial infarction; BP = blood pressure; [creatinine/glucose] = concentration.

and troponin -ve LBBB (data available for 158 [66%] patients) were 8.6% and 9.0%, respectively.

Discussion

Randomized trials of thrombolytic therapy in AMI have shown that mortality reduction is restricted to patients with ST-elevation or LBBB, patients with LBBB deriving the greater benefit.[3] The application of Sgarbossa et al.'s ECG criteria might help to predict 30 d mortality in patients with AMI and LBBB,[7] but their low sensitivity means that they have limited clinical value. Our study has shown that an accurate early diagnosis is difficult in patients with LBBB and cannot be made on the basis of other clinical variables, only the development of LVF showing independent association with infarction. This ensured that fewer than half the patients with LBBB who were given thrombolysis had a discharge diagnosis of AMI and that among patients with a discharge diagnosis of AMI only 29% were given thrombolysis. Treatment rates were lower yet in troponin +ve LBBB. These findings are consistent with registry data that showed that <17% of patients with LBBB and a discharge diagnosis of AMI received reperfusion therapy.[8]

How can rates of reperfusion therapy be improved for patients with LBBB and AMI? Treatment should be given immediately in cases where the LBBB is known to be of new onset.[9] Electronic patient records are potentially valuable in facilitating access to previous ECG reports and the number of these cases should increase. Treatment might also be considered in patients with large troponin elevations (cardiac troponin T>1.1 μg/l), in whom risk is equivalent to CK-based diagnostic thresholds,[10] although there are no trial data to support such a policy and lesser elevations are hard to interpret, particularly when LBBB is associated with pulmonary edema.[11] Waiting for CK analysis or 12 h troponin samples in patients presenting early after the onset of symptoms delays thrombolytic therapy beyond the useful treatment window and is not an option. Nor can a policy of thrombolytic therapy for all patients with chest pain and LBBB be recommended since 77% of the patients in our study did not have AMI and treatment would have exposed them to the unnecessary risk of bleeding complications.

Since our data were recorded, there has been a significant increase in the provision of primary PCI and this might have resulted in a different approach to the treatment of this group of patients. In the UK, for example, the number of centers providing a 24 h primary PCI service has increased from 5 to 23 since 2004, while the number of centers offering daytime only primary PCI has increased from 13 to 37.[12] This has resulted in an almost 10-fold rise in the annual number of primary PCI cases from 405 to 3,930 between 2001 to 2006. In our own Heart Attack Centre, however, patients with LBBB accounted for only 27 (3.3%) of 811 activations between April 2006 to April 2007. It appears, therefore, that clinicians and paramedics are reluctant to put patients with LBBB forward for reperfusion therapy, whether by thrombolytic therapy or PCI, and the likely reason for this is uncertainty over the diagnosis.

Limitations

Data regarding the duration of LBBB (new or old) were not available. Thus, the rate of "appropriate" administration of thrombolytic therapy might have been higher than we have reported. Nevertheless, it is a clinical reality that treatment decisions are usually made without recourse to previous ECGs. We have shown that in "real world" clinical practice most patients treated with thrombolytic therapy on the basis of LBBB at presentation, whether new or old, are diagnosed inaccurately.

Conclusions

In conclusion, our data highlight the difficulty in making an accurate early diagnosis of AMI in patients with LBBB. The majority of those patients with AMI who stand to benefit most from thrombolytic therapy fail to receive treatment, while others without AMI are treated inappropriately. Clinically useful markers of early myocardial infarction are required for this high risk group, but until these are available we believe that the pragmatic management of patients with LBBB and suspected AMI should include urgent coronary angiography with a view to the percutaneous treatment of critical coronary stenoses.

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